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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/297,040	07/21/1999	PETER MOSE LARSEN	2012.0390004	9201

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EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 02/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/297,040	MOSE LARSEN ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-5, 9, 12-18,20,21 and 24-27* is/are withdrawn from consideration.

5)☒ Claim(s) *7-8 and 11* is/are allowed.

6)☒ Claim(s) *10,19,22 and 23* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

Claims 1-27 are pending.

Applicants' amendment filed 17 December 2003, which amends claims 6, 8, 10-11, 19 and 23 has been entered. Also, applicants' request for extension of time of three months has been entered.

Note that in response to the restriction requirement, applicants elect SEQ ID NO:4 (i.e., human galectin-3) for examination which is affirmed by the response filed 17 December 2003, and that the above applicants' election for SEQ ID NO:4 (NEPHGE 298) is an additional election under 35 USC 121, NOT a species election. Therefore, the pending claims 6-8, 10-11, 19 and 22-23 are pending are examined insofar as to the patentably distinct polypeptide of Group II, SEQ ID NO:4, i.e., galectin-3 protein, to which the following is or remains applicable. Claims 1-5, 9, 12-18, 20-21 and 24-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention (see the Office action mailed 17 June 2003). Note that the polypeptides listed in the instant claims 6 and 19 which are not galectin-3 (NEPHGE 298) are drawn to non-elected invention; thus, they are not examined in this Office action.

Also, please note that grounds of objection and/or rejection not explicitly restated and/or set forth below are withdrawn.

Objection to Specification/Claims

The disclosure is objected to because of the following informalities:

In page 48, line 35, change "IL-B" to "IL-1β"; line 37, and change "I" to "one".

In claim 6, after "... diabetes" (item e), the comma "," should be changed to semicolon ";" and before "wherein said diabetes-mediating protein..." should insert "and".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 19 and 22-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of the isolated galetin-3 polypeptide (i.e., SEQ ID NO:4 or NEPHGE 298 listed in Table 1, page 53) and a process of identifying a relation of the galectin-3 to diabetes state via analyzing test sample using electrophoresis (see Example 3, pages 48-49). Applicant is not in possession of a protein that is preventive against diabetes and not in possession of a method of preventing or treating diabetes comprising administering a compound to a subject suffering from the diabetes state.

The instant disclosure recites "a protective protein" (claim 10). Applicants are not in possession of the claimed protein because the specification does not describe prophylaxic ability of galectin-3 protein.

The instant disclosure sets forth "a compound" (see claim 19) being administered to a patient having diabetes symptom. Yet, the instant application does not appear reasonably to provide written description of how the compound NEPHGE 298 (i.e., galectin-3 (SEQ ID NO:4) polypeptide) can be used for treating or preventing diabetes state.

Applicants are not in position of *treating* diabetes comprising administering to a subject suffering from diabetes state galectin-3 protein because the specification does not sufficiently provide in vivo data or/and animal model to demonstrate how to use the claimed galectin-3 for treating diabetes state and there is no apparent indicating relevant animal model for the protein thereof either. Thus, applicants are not in possession of a method of treating diabetes comprising administering to the subject a compound or galectin-3 glycoprotein.

Applicants are not in position of *preventing* diabetes comprising administering to a subject suffering from diabetes state galectin-3 protein The specification does not appear reasonably to provide written description how the galectin-3 has an activity against a diabetes state and how to prevent the diabetes using the galectin-3. The specification provides insufficient guidance or teaching as to how to use the protective protein, e.g., galectin-3 protein, for the diabetes prophylaxis. The specification sets forth that the present invention is directed to a method of preventing diabetes state and that the disclosed protein is useful for predicating diabetes development (see page 15 of the specification). Yet, the specification is silent in how to use the claimed "preventive protein" (e.g., galectin-3 protein) against the diabetes. There are no working examples associated with this regard. The outcome of the prevention or treatment thereof is highly unpredictable, absent the factual indicia to the contrary. Thus, the skilled artisan cannot envision consequence of the preventing diabetes state in the instant claims. As result,

conception cannot be achieved until a representative description of preventing diabetes has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention.

One of skill in the art would reasonably conclude that the disclosure fails to provide written description regarding use of galectin-3 for preventing or treating diabetes disorder. Thus, Applicant was not in possession of make and use of the claimed composition. *See University of California v. Eli Lilly and co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' response to the rejection under 35 USC 112, the first paragraph

The response filed 17 December 2003 argues that the instant disclosure has adequately described what the invention is and how to make and use of SEQ ID NO:4 polypeptide in preventing diabetes state (see page 24). The applicants' argument is found unpersuasive because of the reasons set forth in the above stated ground of rejection.

The response asserts that the specification contains specific teaching regarding the protective effect of SEQ ID NO:4 (galectin-3) protein, e.g., Example 8 details the expression of gelactin-3 in the spontaneous development of diabetes mellitus in a subject (rats), which establishes an animal model for the human diabetes. The applicants' argument is found unpersuasive because of the reasons stated in the above rejection under 35 USC 112, the first paragraph, and because although Example 8 shows galectin-3 expression on a diabetes-prone animal, the example provides insufficient information or factual indicia which clearly establish a role or potential of galectin-3 in

treating or/and preventing the diabetes state. Note that galectin-3 expression patterns: down-regulation (*in vivo*) at day 7, onset of a diabetes state, IDDM *versus* up-regulation (*in vitro*) in IL-1β stimulated islets from where insulin secrete) does not appear to contribute to or suggest role of galectin-3 in treating or/and preventing the diabetes state. IL-1β potently inhibits insulin secretion. Since the instant disclosure does not teach galectin-3 antagonism to the IL-1β action (inhibiting insulin secretion) or galectin-3 involvement of an event, e.g., insulinotropism, during development of the diabetes IDDM, Example 8 does not support the galectin-3 treatment or prevention of the diabetes. In addition, the above-mentioned *in vitro* and *in vivo* information of regulating galectin-3 expression appears not comparable form each other because the *in vivo* information should not be compared with the *in vitro* when evaluating pharmaceutical data. Further, because the claimed protein has contradictory properties, i.e., "protective" (a positive role, see claim 10) and "deleterious" (a negative role, see claim 11), in treating or preventing diabetes state, galection-3 protein that is claimed to be a preventive protein against diabetes is unpredictable in this regard. Absent is the explanation or/and guidance regarding upon which property of the claimed protein, the information of Example 8 can be reasonably understood and interpreted. Thus, in light of the above statements, Example 8 is not evident for supporting the claimed subject matter.

Also, the response discusses the issue with regard to a negative role of galectin-3 in development of diabetes which is suggested by Pugliese et al. reference. The response argues that the reference is uncertain of the galectin-3 role in diabetes and does not suggest galectin-3 has a protective or deleterious effect on the diabetes state; thus, the response infers that the reference provides no reason to contradict the present invention (see pages 25-26). The applicants' argument is unpersuasive. Pugliese et al. does teach involvement of galectin-3 in diabetes state as is

evidenced by the fact that galectin-3 expression was observed during development of diabetes disease and the diabetic milieu induces galectin-3 production (see abstract and Figure 1D). More importantly, Pugliese et al. teach that galectin-3 involves in pathogenesis of glomerulopathy during diabetes development due to the multifunctional nature of the lectin galectin-3 (see the 2nd paragraph, the left column, page 1256). It is thus a burden for applicants to show that the factual indicia provided by Pugliese et al. is disputable and neglectable. Since, contrary to the current application that sets forth galectin-3 preventing diabetes state, the Pugliese et al. reference teaches non-preventive role of galectin-3 in the diabetes development, the applicants' argument stated above is therefore deemed unpersuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 19 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 recites the limitation "said diabetes-mediating protein". There is insufficient antecedent basis for this limitation in the claim. Also, claim 19 is indefinite in "a compound"; it is unclear as to whether or not the recited compound refers to any organic or inorganic compound, or biomolecule. The dependent claims are also rejected.

Conclusion

Claims 6, 10, 19 and 22-23 are not allowed, and claims 7-8 and 11 are free from prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

Samuel Wei Liu, Ph.D.

January 27, 2004

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER